UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,785	10/03/2005	Marco Cattaruzza	DEBE:053US	1068

32425 7590 02/01/2008
FULBRIGHT & JAWORSKI L.L.P.
600 CONGRESS AVE.
SUITE 2400
AUSTIN, TX 78701

EXAMINER	
WOLLENBERGER, LOUIS V	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
02/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,785	CATTARUZZA ET AL.	
	Examiner	Art Unit	
	Louis V. Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1 and 2* is/are allowed.

6)☒ Claim(s) *3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 11/29/07 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 5/31/07 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 11/29/07, claims 1-3 are pending and under examination.

Specification/Sequence Compliance

The disclosure is objected to because of the following: This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The specification as filed does not comply with the requirements above, in particular 1.821(d) at least, because it contains nucleotide sequences of ten or more nucleotides that are not identified by accompanying sequence identifiers.

In particular, the sequence set forth at page 14, line 14, of the specification. Applicants are advised to review the entire application—claims, drawings, and specification—for complete

compliance with the Sequence Rules. Thus, the Examiner notes herein that the above citation ,which sets forth examples in the specification of nucleotide sequences that require SEQ ID NO:, is by way of illustration. In order to be fully responsive to this Office Action, Applicant should review this application in its entirety to ensure compliance with the requirements of 37 CFR 1.821 through 1.825 and to make all appropriate corrections.

Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g).

***

Applicant is further advised the Wattanapitayakul et al. paper cited at page 8 of the specification is reported by Medline to have been published in 2001, not 2000 as cited in the specification.

Claim Rejections - 35 USC § 102—withdrawn

The rejection of Claims 1 and 2 under 35 U.S.C. 102(b) as being anticipated by Zhang et al. (1995) *J. Biol. Chem.* 270:15320-15326 is withdrawn in view of Applicant's amendment to claim 1. The amendment is supported by the disclosure at paragraph 34 of the instant pre-grant publication (US 20060122134 A1), corresponding to page 17 of the specification.

Claim Rejections - 35 USC § 112, first paragraph—maintained

Claim 3 remains rejected under 35 U.S.C. 112, first paragraph, for the reasons of record because the specification, while being enabling for methods of treating coronary heart disease and rheumatoid arthritis comprising administering an oligonucleotide decoy comprising SEQ ID

NO:17, does not reasonably provide enablement for methods of treating any of the several other diseases recited in or embraced by claim 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 11/29/07 have been fully considered but are not persuasive.

The Declaration under 37 CFR 1.132 filed 11/29/07 is insufficient to overcome the rejection of claim 3 based upon reasons set forth in the last Office action.

1. While Applicant's amendment to the claim removes a large number of non-enabled embodiments, the claim remains extremely broad embracing a multitude of methods for treating any inflammatory and autoimmune disease, which, as a whole, are not considered to be enabled for at least those reasons previously given.
2. Counsel's arguments and Applicant's sworn statements, submitted in a 1.132 Declaration, are unsubstantiated by evidence showing or demonstrating a link between the human eNOS -786 polymorphism and a representative number of autoimmune diseases and inflammatory diseases. Further, no link is found associating the polymorphism with vasculopathy or atherosclerosis in general, a disease that may be multifactorial in origin, nor is there sufficient evidence to show the claimed decoys could be used at the time of filing to treat acute conditions such as cardiac infarction, heart failure, cerebral disorders, stroke, dementia, and occlusions without engaging in undue experimentation. In the absence of objective evidence, the arguments and statements submitted amount to little more than an

opinion. There is reason to doubt the objective truth of the asserted statements, since no sound evidence (e.g., data) has been put forward linking the polymorphism with the genus of diseases targeted.

3. The claimed decoy (comprising SEQ ID NO:17) is a C-type decoy, designed to treat diseases associated with the -786 T to C transition in the eNOS gene. See the definition at page 6 of the specification, and disclosure at page 3147 of Melchers et al. (2006) Arthritis Rheum. 54:3144-3151.

4. The single nucleotide C to T transition polymorphism at positions -786 of the human eNOS gene has been convincingly correlated to coronary heart disease and rheumatoid arthritis. See Wattanapitayakul et al. (2001) Trends Pharmacol. Sci. 22:361; Cattaruzza et al. (2004) Circ Res. 95: 841-847, 2004; and Melchers et al. (2006) Arthritis Rheum. 54:3144-3151. See also the specification at page 10; and Tables 1 and 2, pages 31-32. And see the Declaration submitted under 37 CFR 1.132 filed 4/13/07. Evidence referred to therein shows the uptake and delivery of double stranded decoys into bronchial epithelium in mice when administered intranasally and into psoriatic skin when administered topically. That Declaration, however, does not address issues concerning the nexus between the eNOS ^{786}C/T SNP, SEQ ID NO:17, and the many diseases now recited, and is therefore not remedial to this portion of the rejection, as explained above.

5. Delivery of decoys to vascular cells in vivo with a resulting therapeutic effect has been demonstrated in at least one instance, suggesting that means for delivering decoys into the vasculature in an amount necessary to produce a therapeutic effect

can be achieved without undue experimentation. See Morishita et al. (1995) Proc. Natl. Acad. Sci. (1995) 92:5855-5859; and Morishita et al. (1998) Circ. Res. 82:1023-1028. Delivery of decoys to tissues affected by arthritis would also appear to be enabled at the time of filing. See Tomita et al. (2003) Gene therapy for arthritis Curr Drug Targets. 2003 Nov;4(8):609-12, for example.

6. Accordingly, the instant claim remains rejected for being drawn to non-enabled embodiments, because, aside from coronary heart disease and rheumatoid arthritis, the specification does not reasonably suggest a correlation between the claimed decoys, target polymorphism and a representative number of the diseases recited in or embraced by the claims. As a result, there is reason to doubt whether the claimed decoys could be used to treat the full scope of diseases recited without undue experimentation.

Allowable Subject Matter

Claims 1 and 2 are free of the prior art searched to date.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis V. Wollenberger whose telephone number is 571-272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LW
January 22, 2008
Examiner, Art Unit 1635

/Sean McGarry/
Primary Examiner
AU 1635

Notice to Comply	Application No.	Applicant(s)	
	10527785	CATTARUZZA ET AL.	
	Examiner	Art Unit	
	Louis V. Wollenberger	1635	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: See accompanying Office Action, citing sequence at page 14, line 14, of the specification. The sequence is not identified with a SEQ ID NO:.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the specification**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
For CRF Submission Help, call (571) 272-2501/2583.
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY